25. (New) The method of Claim 14 wherein the fluorescent labels comprise dendrimer labels.

26. (New) A method of simultaneously genotyping multiple samples, the method comprising:

amplifying a genomic segment comprising a genetic locus from a plurality of samples using polymerase chain reaction primers;

forming a microarray on a surface from the amplified genomic segments, wherein each location on the surface contains material derived from a single sample;

hybridizing the microarray with a mixture of labeled synthetic oligonucleotides, wherein the mixture comprises oligonucleotides complementary to the genomic segment; and

deriving genotyping information for the plurality of samples simultaneously by detecting signals from the hybridized microarray to thereby genotype the multiple samples.

REMARKS

Claims 1-24 were pending in the application, all of which stand rejected. In this action Claims 1, 8-10, 13-15, and 17 are amended, Claim 2 has been cancelled and new Claims 25 and 26 have been added. Reconsideration and allowance is respectfully requested in view of the above amendments and following remarks.

Claim rejections under 35 U.S.C. §112(2)

The second element of Claim 1 has been amended to recite

"forming a microarray on a surface from the amplified genomic segments, wherein each location on the surface contains amplified material derived from a single sample and consisting essentially of a single genomic segment;"

The language objected to in paragraphs 2(a) and 2(b) of the Office Action has been replaced rendering the specific rejection of those paragraphs moot. The spirit of the rejection, requiring the relationship between the material on the surface and the genomic segments has been met by the amendments to Claim 1.

The third element of Claim 1 recites

LAW OFFICES OF
SKJERVEN MORRILL
MACPHERSON LLP

25 METRO DRIVE
SUITE 700
SAN JOSE, CA 95110
(408) 453-9200
FAX (408) 453-7979

"hybridizing the microarray with a mixture of labeled synthetic oligonucleotides, wherein the mixture comprises oligonucleotides complementary to the genomic segments;"

Paragraph 2(c) suggested amending Claim 1 to define the relationship between "mixture", "amplified genomic segments" and "material on the microarray". Applicants respectfully submit Claim 1, as amended which recites each "location on the surface contains amplified material derived from a single sample and consisting essentially of a single genomic segment" and a mixture which "comprises oligonucleotides complementary to the genomic segments" provides the required relationships.

Claim 1 has been amended to recite "to thereby genotype the multiple samples" at the final claim element and to insert "labeled" in front of synthetic oligonucleotides, satisfying the requirements of paragraphs 2(d) and 2(e). Claim 2 has been cancelled rendering the rejection of Claim 2 moot. Claim 8 has been amended as recommended in paragraphs 2(g) and 2(h). Accordingly, Applicant submits, the claims, as amended, satisfy the requirements of 35 U.S.C. §112(2).

Rejection of Claims 1-3, 8-9, 12-13, 15-16, and 21 under 35 U.S.C. §102(b) as anticipated by Wang

The rejection is respectfully traversed. For purposes of examination, the Examiner interpreted Claim 1 to recite "genomic segments are amplified to thereby produce synthetic oligonucleotides which are hybridized to the material on the array." (Office Action, page 4) For the record, Applicant respectfully notes this is not the correct interpretation of Applicant's Claim 1. As recited in Claim 1, each location on the surface contains amplified material derived from a single sample and consisting essentially of a single genomic segment." Note the teaching of the specification at page 6 lines 16-17 "Each spot in the microarray corresponds essentially to a single amplicon from a single individual, within the precision of PCR [polymerase chain reaction] processes." Applicant submits, as conventionally understood, PCR amplification does not produce synthetic oligonucleotides.

Under the incorrect assumption discussed above, the office action argues that Wang on page 1078, right column, first full paragraph discloses all the elements of Applicant's Claim 1. The distinctions between the present Claim 1 and Wang and the references cited elsewhere in the Office Action, may be understood with respect to three distinct elements: (1) the

LAW OFFICES OF
SKJERVEN MORRILL
MACPHERSON LLP

25 METRO DRIVE
SUITE 700
SAN JOSE, CA 95110
(408) 453-9200
FAX (408) 453-7979

material on the microarray, (2) the material hybridized to the microarray, and (3) the information derived simultaneously from one microarray- number of samples and number of loci for which information is obtained.

In the present case, (1) the material at each location on the microarray is "amplified material derived from a single sample and consisting essentially of a single genomic segment," "each genomic segment comprising a distinct genetic locus;" (2) the material hybridized to the microarray is "a mixture of labeled synthetic oligonucleotides .. complementary to the genomic segments," and (3) the information derived is "genotyping information" derived "simultaneously for the plurality of samples at the plurality of genetic loci."

In contrast, in Wang, 149 distinct variant detector array (VDA) chips are used, each containing 150,000 to 300,000 features, where a VDA is an example of a "DNA chip" "produced with parallel light-directed chemistry to synthesize specified oligonucleotides probes covalently bonded at defined locations on a glass surface or 'chip.'" (page 1078) In Wang, (1) the material at each location on the array is a specific sequence of synthetic oligonucleotides. (2) The material hybridized to the microarray is "corresponding STSs" [sequenced tagged sites] amplified from an individual, pooled together, labeled with biotin ..." (page 1078, right column, emphasis added) Since "16,725 STSs covering 2 Mb of human DNA" were studied with 149 distinct chip designs, the material hybridized to a single array contains multiple STSs from a single individual. (3) The information derived simultaneously is classification of an individual sample as "homozygous for the expected sequence, homozygous for an alternative sequence, or heterozygous" for multiple different sequences. The outcome of the study was "A collection of 2748 candidate SNPs [single nucleotide polymorphisms] were identified." (page 1078, right column, 2nd paragraph)

Since the present Claim 1 distinguishes from Wang by reciting different material at each location on the microarray, hybridizing the microarray with different material, to obtain different information, the present Claim 1 is not anticipated by Wang. Claims 3, 8-9, 12-13, 15-16, and 21 are dependent directly or indirectly on Claim 1 and therefore are allowable for at least the reason Claim 1 is allowable. Claim 2 has been cancelled rendering the rejection of Claim 2 moot.

LAW OFFICES OF
SKJERVEN MORRILL
MACPHERSON LLP

25 METRO DRIVE
SUITE 700
SAN JOSE, CA 95110
(408) 453-9200
FAX (408) 453-7979

Rejection of Claims 1, 2, 8, 12, 21, and 24 under 35 U.S.C. §102(b) as anticipated by Lashkari

The rejection is respectfully traversed. The Office Action (page 6) characterizes Lashkari (page 13057, left column, last paragraph - right column, first paragraph) as disclosing all of the elements of Applicant's Claim 1. Applicant submits this characterization of Lashkari is not accurate. The cited passage of Lashkari describes automatically synthesizing PCR primers to amplify desired ORFs [open reading frames] from genomic DNA of yeast. "The products were arrayed using a high-density DNA arrayer. The gene arrays can be used for hybridization with a variety of labeled products such as cDNA for gene expression analysis or genomic DNA for strain comparisons." (page 13057, right column) Applying the analysis of the previous section, (1) the material on the array disclosed by Lashkari is one ORF/location derived by PCR from yeast whole genomic DNA. (2) The material hybridized to the array is labeled cDNA or labeled genomic DNA (also see page 13058, first column); and (3) The information derived simultaneously is a comparison between cDNA and genomic DNA at multiple ORFs for gene expression analysis or comparison between genomic DNA for two different strains at multiple ORFs.

In contrast, as described above, the present Claim 1 recites (1) a microarray, which at each location has "amplified material derived from a single sample and consisting essentially of a single genomic segment," hybridized with (2) "a mixture of labeled synthetic oligonucleotides" to (3) derive "genotyping information simultaneously for the plurality of samples at the plurality of genetic loci." Since Applicant's Claim 1 distinguishes over Lashkari by at least these three elements, Claim 1 is allowable over Lashkari. Claims 8, 12, 21, and 24, which are dependent directly or indirectly on Claim 1 are allowable for at least the reason Claim 1 is allowable. Claim 2 has been cancelled rendering the rejection of Claim 2 moot.

Rejection of Claims 1-4, 12-18, 21 and 24 under 35 U.S.C. §103(a) as unpatentable over Wang in view of Brown

The rejections over Wang in view of Brown are respectfully traversed. The distinctions between the present Claim 1 and Wang have been described above. The Office Action on page 8, lines 3-8 also characterizes Brown (Column 15, lines 19-43) as disclosing all the elements of Applicant's Claim 1. Applicant submits such a characterization is not accurate. Brown discloses "96 identical ... microarrays fabricated on a single ... sheet of

LAW OFFICES OF
SKJERVEN MORRILL
MACPHERSON LLP

25 METRO DRIVE
SUITE 700
SAN JOSE, CA 95110
(408) 453-9200
FAX (408) 453-7979

plastic-backed nitrocellulose where each microarray could contain, for example, 100 DNA fragments representing all known mutations of a given gene. The region of interest from each of the DNA samples from 96 patients could be amplified, labeled, and hybridized to the 96 individual arrays." (Col. 15, lines 23-29)

Again applying the three-element analysis presented above, in Brown, (1) the material at each location of each of the identical microarrays is a DNA fragment representing a known mutation; (2) the material hybridized to a single array is an amplified, labeled portion of DNA from an individual patient; and (3) the information obtained from a single array is identification of a mutation in a given gene for a single patient. Brown, therefore, does not disclose any of the elements of Applicant's Claim 1. Since neither Wang nor Brown disclose the elements of the present Claim 1, the combination of Wang with Brown similarly does not teach or suggest the present Claim 1. Claim 1 is thus allowable over Wang in view of Brown. Claims 8, 9, 12-18, and 21-24, which depend directly or indirectly on Claim 1 are allowable for at least the reason Claim 1 is allowable.

Rejection of Claims 5-7 and 11 under 35 U.S.C. §103(a) as unpatentable over Wang in view of Cheng

As presented above, Applicant's Claim 1 is allowable over Wang. The Office Action (page 10, paragraph 8) describes Cheng as teaching "a similar method for simultaneously genotyping multiple samples comprising: amplifying genomic segments; forming a microarray; hybridizing the microarray with a mixture of synthetic nucleotides ..." (page 562, right column last paragraph) Applicant respectfully submits the method of Cheng is not similar to the method recited in present Claim 1. In the cited passage, Cheng teaches patient samples are amplified with two different combinations of PCR primer pairs. "Each PCR product pool is then hybridized to the corresponding panel of oligonucleotide probes that have been immobilized in a linear array on backed, nylon membrane strips." Cheng does not use a microarray. The material on probe strips is synthetic oligonucleotides, the probe strips are hybridized with labeled amplified genomic material resulting from amplification with multiple primer pairs, one patient sample per probe strip. Cheng, therefore, does not remedy the defects of Wang with respect to Claim 1. Claim 5-7 and 11, which depend on Claim 1 are allowable for at least the reason Claim 1 is allowable.

LAW OFFICES OF
SKJERVEN MORRILL
MACPHERSON LLP

25 METRO DRIVE
SUITE 700
SAN JOSE, CA 95110
(408) 453-9200
FAX (408) 453-7979

Additional Rejections under 35 U.S.C. §103(a)

The rejection of Claim 10 as unpatentable over Wang is respectfully traversed. Claim 10 is dependent on Claim 1 and is allowable for at least the reasons Claim 1 is allowable. Claims 19-20 were rejected as unpatentable over Wang in view of Brown and Fodor. The distinctions of Claim 1 over Wang and Brown have been discussed above. Fodor fails to remedy the defects of Wang and Brown with respect to Claim 1. Consequently Claim 1 and Claims 19-20 dependent therefrom are allowable over Wang and Brown in view of Fodor. Similarly, Claims 22-23 are allowable over Wang in view of Pease. Pease does not remedy the defects of Wang with respect to Claim 1. Therefore, Claim 1, and Claims 22-23 dependent therefrom, are allowable over Wang in view of Pease.

New Claims 25 and 26

Support for new Claims 25 and 26 is found throughout Applicant's specification. In particular, support for Claim 25 is found at page 9, lines 13-14 of the specification. Claim 25 is dependent on Claim 1 and is therefore allowable for at least the reasons Claim 1 is allowable.

New Claim 26 recites the elements

> "amplifying a genomic segment comprising a genetic locus from a plurality of samples using polymerase chain reaction primers;
>
> forming a microarray on a surface from the amplified genomic segments, wherein each location on the surface contains material derived from a single sample;
>
> hybridizing the microarray with a mixture of labeled synthetic oligonucleotides, wherein the mixture comprises oligonucleotides complementary to the genomic segment;"

As discussed above, none of the cited references teach or disclose a microarray in which each location on the surface of a microarray contains material comprising a single genetic locus from a single sample and hybridizing the microarray with a mixture of labeled synthetic oligonucleotides to derive "genotyping information for the plurality of samples simultaneously." Therefore, new Claim 26 is distinguished from the cited references.

LAW OFFICES OF
SKJERVEN MORRILL
MACPHERSON LLP

25 METRO DRIVE
SUITE 700
SAN JOSE, CA 95110
(408) 453-9200
FAX (408) 453-7979

Conclusion

Accordingly, for at least the above reasons, Claims 1, and 3-26, the claims pending in the application are in condition for allowance and prompt passage to allowance is respectfully requested. Should the Examiner wish to discuss any aspect of the present application, the Examiner is invited to telephone either the undersigned Agent for Applicants or, alternatively, Michael Halbert at (408) 453-9200.

EXPRESS MAIL LABEL NO.

EL 797 672 536 US

Respectfully submitted,

Roberta P. Saxon
Agent for Applicants
Reg. No. 43,087

LAW OFFICES OF
SKJERVEN MORRILL
MACPHERSON LLP

25 METRO DRIVE
SUITE 700
SAN JOSE, CA 95110
(408) 453-9200
FAX (408) 453-7979

ATTACHMENT A

In the following, insertions are underlined and deletions are enclosed in brackets.

1. (Amended) A method of simultaneously genotyping multiple samples, the method comprising:

amplifying a plurality of genomic segments from a plurality of samples using a plurality of polymerase chain reaction primers, each genomic segment comprising a distinct genetic locus;

forming a microarray on a surface from the amplified genomic segments, wherein [material at] each location on the surface contains amplified material derived from a single sample and consisting [corresponds] essentially [to] of a single genomic segment [from a single sample];

hybridizing the microarray with a mixture of labeled synthetic oligonucleotides, wherein the mixture comprises oligonucleotides complementary to the genomic segments; and

deriving genotyping information simultaneously for [multiple] the plurality of samples at the plurality of genetic loci [simultaneously] by detecting signals from the hybridized microarray to thereby genotype the multiple samples.

8. (Amended) The method of Claim 1 wherein the [density of the microarray on the] surface [is] of the microarray comprises at least 1000 [spots] locations per square centimeter.

9. (Amended) The method of Claim 1 wherein the mixture of labeled synthetic oligonucleotides comprises ten different oligonucleotide sequences.

10. (Amended) The method of Claim 1 wherein the labeled synthetic oligonucleotides are between about 10 and about 30 nucleotides in length.

13. (Amended) The method of Claim 1 wherein hybridizing is performed at a temperature about 10 °C below the melting temperature of the labeled synthetic oligonucleotides.

LAW OFFICES OF
SKJERVEN MORRILL
MACPHERSON LLP

25 METRO DRIVE
SUITE 700
SAN JOSE, CA 95110
(408) 453-9200
FAX (408) 453-7979

14. (Amended) The method of Claim 1 wherein the labeled synthetic oligonucleotides comprise fluorescent labels.

15. (Amended) The method of Claim 1 wherein the labeled synthetic oligonucleotides comprise non-fluorescent labels.

17. (Amended) The method of Claim 14 wherein the signals are generated by fluorescence emission from the labeled synthetic oligonucleotides.

LAW OFFICES OF
SKJERVEN MORRILL
MACPHERSON LLP

25 METRO DRIVE
SUITE 700
SAN JOSE, CA 95110
(408) 453-9200
FAX (408) 453-7979